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Letter to the editor

How safe are carmustine wafers?

1. Introduction

Glioblastoma multiforme (GBM) is generally considered the most aggressive form of brain tumor [1] and, for decades, the standard therapeutic strategy has been based on complete tumor removal followed by radiotherapy and/or systemic chemotherapy [2]. Yet, despite such invasive treatments, the survival of patients who have GBM remains low, with 5-year survival rates of 5% [3]. One possible explanation for this lack of success is that the blood–brain barrier (BBB) prevents chemotherapy from reaching the tumor bed at meaningful concentrations [4]. For this reason, since the mid-1990s [4], placing wafers loaded with carmustine, a nitrosourea oncolytic agent, in the resection cavity has been proposed. However, this strategy has demonstrated only slight benefits in the treatment of newly diagnosed [5–7] and recurrent [4] high-grade gliomas, with a reduction in mortality of 20–30% [8]; indeed, in the subgroup of patients with GBM, overall survival failed to reach statistical significance compared with the use of placebo wafers [8]. Moreover, several complications have been reported with the use of carmustine wafers, including infection and local edema [9–11], as well as the development of symptomatic cysts responsible for significant morbidity [10,12,13]. Therefore, the use of carmustine wafers and management of their complications remain controversial [14,15].

In this case report of a patient who presented with a cerebral reactive cyst after carmustine wafer implantation for recurrent glioma, the evolution of which was favorable after administration of high-dose corticosteroids, we also include a literature review of the incidence, risk factors and management of carmustine wafer complications in cases of high-grade glioma.

2. Case report

A 59-year-old patient was operated on for recurrent left parietal GBM. The initial diagnostic circumstances were contralateral numbness associated with weakness, graded as 4/5 in both the lower and upper limbs, and seizures. First-line treatment included complete tumor removal and concomitant radiochemotherapy with temozolomide, according to the Stupp protocol [16]. Six months after the initial surgery, follow-up imaging performed in the absence of symptoms showed tumor extension with contrast enhancement. This prompted a second operation for carmustine wafer implantation, a decision taken during a multidisciplinary clinic, followed by second-line chemotherapy including bevacizumab (Fig. 1). However, 4 weeks after this second surgery, the patient developed progressive right hemiparesis, which was graded 3/5 at examination. Brain magnetic resonance imaging (MRI) was then performed (Fig. 2) and revealed hypointense signals on T1-weighted sequences and hyperintense signals on T2-weighted sequences in the resection cavity, with ring enhancement after gadolinium contrast administration. Diffusion-weighted imaging (DWI) sequences showed no signal restriction.

In the absence of arguments for brain abscess, the diagnosis of cerebral reactive cyst was retained. The patient

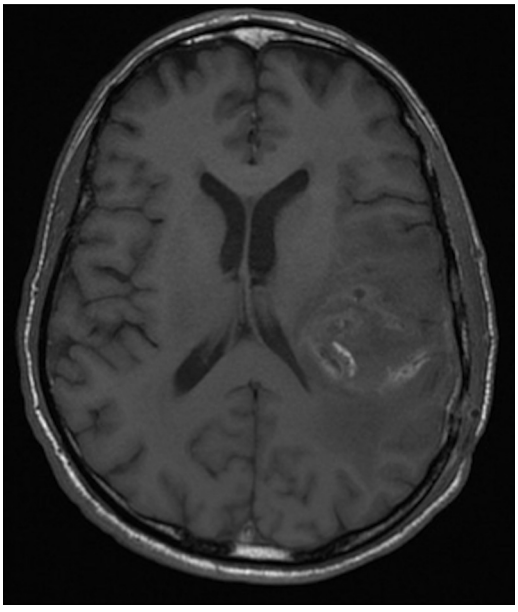

Fig. 1 – Postoperative axial T1-weighted magnetic resonance imaging (MRI) of the brain shows complete tumor resection and implanted carmustine wafers.

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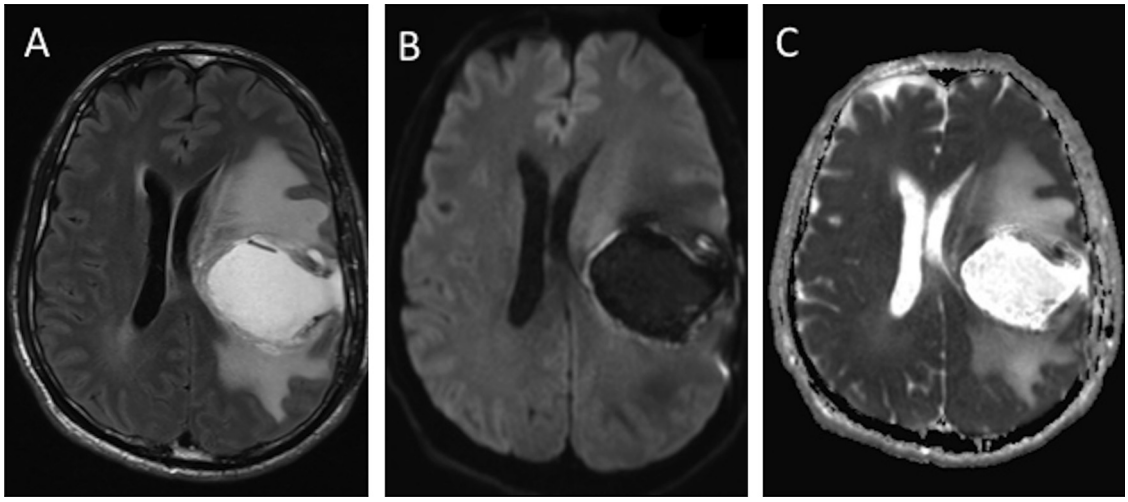

Fig. 2 – Axial MRI of (A) a T2-weighted fluid-attenuated inversion recovery (FLAIR) sequence and (B) diffusion-weighted imaging (DWI) at b1000 reveal a large cyst in the resection cavity with a major mass effect, but (C) no restriction of the apparent diffusion coefficient (ADC) on DWI.

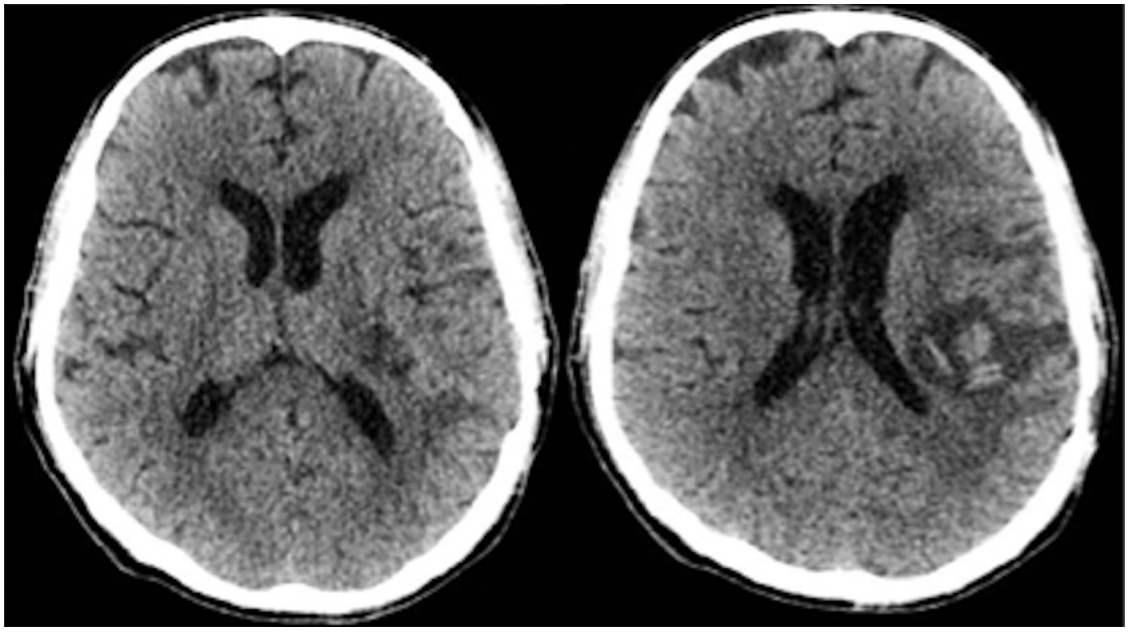

Fig. 3 – Axial cerebral computed tomography (CT) scans with no contrast enhancement, taken 1 month after corticosteroid administration, show a decrease in cyst volume and no residual mass effect.

was placed on intravenous (IV) dexamethasone 60 mg every 8 h for 1 week, followed by a gradual 50% dose reduction every week for 1 month until complete cessation of the corticosteroid. The clinical evolution was favorable after such corticosteroid treatment, with major regression of weakness protecting against surgical cyst decompression. Follow-up imaging showed decreases in cyst volume and mass effect (Fig. 3), and the patient remained clinically stable for several months. Unfortunately, despite intensification of the chemotherapy protocol with the use of bevacizumab, the patient died 18 months after the initial diagnosis.

3. Literature review

As our case report involved symptomatic cerebral cyst following carmustine wafer implantation, we reviewed the literature through a PubMed search using the key terms 'carmustine wafers cyst' and 'carmustine wafers complications', which retrieved 35 peer-reviewed articles investigating patients with carmustine wafer implantation. Articles not evaluating carmustine wafer complications were excluded. Of those 35 papers, 17 involving 1424 patients with carmustine

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